ISSN: 2832-7705

Case Report

International Journal of Clinical and Medical Education Research

Lipid profile and pulmonary ultrasound in PIMS. Three case reports

Angelo M. Acquafredda[1], Chiara Lorusso[1], Anna L. S. Di Giovinazzo[1], Anna Maria Pastoressa[1], Maria Simone[1], Stefania Mastromattei[1*], Maurizio Specchio[1], Pietro Cialdella[1], Pamela Vitullo[1].

[1]Pediatrics and Cystic Fibrosis Unit, Hospital "G. Tatarella "- Cerignola (ASL FG)

[*]Corresponding author
Stefania Mastromattei, 1Pediatrics and Cystic Fibrosis Unit, Hospital "G. Tatarella "- Cerignola (ASL FG).

Submitted: 24 Jul 2022; **Accepted**: 28 Jul 2022; **Published**: 06 Aug 2022

Citation: *Stefania Mastromattei., Chiara Lorusso., Mara Simone., Maurizio Specchio., Pamela Vitullo. (2022). Lipid profile and pulmonary ultrasound in PIMS. Three case reports. Int J Clin Med Edu Res. 1(2), 84-88.*

Abstract

SARS-CoV-2 infection in children often occurs in an asymptomatic and/or paucisymptomatic manner. However, a multisystem inflammatory syndrome (MIS-C) may occur in the 4-6 weeks following the infection. This syndrome is triggered by the release of cytokines, due to an abnormal immune response to the infection. The recent literature described the different clinical spectrum and phenotypic features of MIS-C, but there are few data about the characteristics of the syndrome after clinical recovery phase. The description of three cases of post-SARS-CoV-2 infection syndrome in children aims to providing evidence of the relevant follow-up phase, besides the onset symptoms and the clinical course. In two cases, the onset clinical symptoms were similar to Kawasaki syndrome, while in the third one neurological impairment was prevalent. No association with gastrointestinal symptoms was found, while the increase in the inflammation and phlogosis indices was constant. Cardiac involvement was never reported, despite the positivity of myocardial distress markers, while the lung ultrasound showed signs of interstitial disease, even though there were no clinical respiratory signs. In all cases, the course was benign with improvement of clinical conditions within about 5 days and normalization of phlogosis indices and lung involvement after about 30 days from the onset. The lipid profile at onset was characterized by an increase in triglyceride levels, thus suggesting a relation with the inflammation indices, followed by an increase in the total cholesterol - probably related to the immune response - after the clinical healing phase, contrary to what has been stated by the current literature.

Keywords: Covid-19 Infection, Multisystem Inflammatory Syndrome (Mis), Case Report, Lipid Profile, Follow-Up.

Introduction

SARS-CoV-2 infection in children, unlike in adults, often occurs in an asymptomatic and/or paucisymptomatic manner. However, in some cases, a multisystem inflammatory syndrome (MIS-C) may occur in the 4-6 weeks following the infection [1, 2]. This syndrome, described both in the USA and in Europe, roughly occurs in 0,6% of all Covid-19 infection cases in patients with an average age of 8,6 years (from 3 months to 20 years old) and is triggered by the release of cytokines, due to an abnormal immune response to the infection [3, 4]. MIS-C is defined by the presence of persistent fever associated with gastrointestinal and/or respiratory symptoms, mucocutaneous manifestations, inflammation and organ dysfunction and evidence of past or recent Covid-19 infection, excluding other microbial causes. It overlaps with other inflammatory diseases like Kawasaki syndrome (KS) or toxic shock syndrome and has some similar features. Its course is potentially severe, but the mortality rate is low (2%) [5]. The American College of Rheumatology (ACR) [6] recommends the use of intravenous immunoglobulins (IVIg) and/or high-dose of corticosteroids as first-line treatment; about 30% of patients can also require an immunomodulatory therapy in order to keep the inflammation under control. Other therapies that have been used include the second dose of IVIg, anakinra, tocilizumab and infliximab [7, 8].

Although the clinical spectrum, the phenotypic features and the treatment of MIS-C have been extensively described, there are few data about the characteristics of this syndrome after the clinical recovery phase. The description of these three cases of post-SARS-CoV-2 infection syndrome in children aims to providing evidence of the relevant follow-up phase, besides the onset symptoms and the clinical course.

Case Reports

Case 1: 14-month-old child with negative past medical history and normal weight-for-stature growth, hospitalized for 5 days for hyperpyrexia with highest peaks of 39,7°C and poor response to common antipyretic therapies, asthenia and feeding difficulties. The child was in fair general condition, vigilant and responsive, with fever without signs of meningeal irritation, skin pallor,

pharyngeal hyperemia with fibrin deposition on the right tonsil. During the hours straight after the hospitalization, he showed extreme drowsiness together with slight neck rigidity and photophobia. Therefore, a computerized axial tomography of the brain and brainstem and an examination of the fundus oculi were performed and both of them were normal. The lumbar puncture for CSF examination wasn't performed, as the symptoms of meningism disappeared rapidly and general health conditions improved. Blood chemistry tests revealed lymphocytopenia, an increase in phlogosis and inflammation indices, an impressive growth of triglyceride levels as well as the total cholesterol value, while HDL and LDL were normal. The nasopharyngeal swab for SARS-COV-2 was negative, but IgM and IgG antiSARS-COV-2 (IgG>IgM) were observed. Among the instrumental examinations, the chest X-ray, the ECG and the echocardiogram were normal, while the lung ultrasound showed signs of interstitial disease in the left parasternal site. An antibiotic therapy with Ceftriaxone (100mg/kg/day iv) and cortisone therapy with Methylprednisolone (1mg/kg/day iv) were performed for 5 days, with the progressive improvement of the general clinical conditions and the symptoms resolution within 4-5 days upon entry. After 1 month, the hematochemical parameters normalized - except for the increase of IgG for SARS-COV2 by 50% and the increase of the total cholesterol value – as well as the instrumental ones.

Case 2: 3-years and 11-months old child with negative past medical history and normal weight-forstature growth, hospitalized for hyperpyrexia over 4 days with poor response to common antipyretic therapies and antibiotics as macrolides. The patient was in bad general condition with fever without signs of meningeal irritation. He showed signs of conjunctival hyperemia with cheilitis, pharyngeal hyperemia, appearance of maculo-papular rash in the supraorbital and pretibial region, as well as cheeks, back, palm and soles, lateral cervical and retronucal lymphadenopathy. Blood chemistry tests revealed lymphocytopenia associated with thrombocytopenia, an increase in phlogosis and inflammation indices, as well as triglyceride levels, while the total cholesterol value, HDL and LDL were normal. The nasopharyngeal swab for SARS-COV-2 was negative, while the serology was positive (IgG>IgM). The chest X-ray and the cardiac instrumental assessment were normal, while the lung ultrasound showed signs of interstitial disease in the left parasternal site. An antibiotic therapy with Ceftriaxone (100mg/kg/day iv) and cortisone therapy with Methylprednisolone (1mg/kg/day iv) were performed for 5 days, together with intravenous immunoglobulins (1g/kg/day iv) for 2 days.

The general clinical conditions progressively improved and after about 5 days from admission there was a complete resolution of symptoms and the normalization of the instrumental examinations and of hematochemical parameters, except for the increase of the total cholesterol value and of the IgG for SARS-COV2 by 50%.

Case 3: 1-year and 6-months-old child with negative past medical history and normal weight-forstature growth, hospitalized for fever over 5 days with poor response to common antipyretic therapies associated with cough. He was vigilant and responsive with fair general clinical conditions and he had fever without signs of meningeal irritation. Moreover, he showed conjunctival hyperemia with cheilitis, maculo-papular rash on the trunk and back of the feet and sour vesicular murmur widespread on chest auscultation. Blood chemistry tests revealed lymphocytopenia, an increase in phlogosis and inflammation indices, as well as triglyceride levels, while the total cholesterol value, HDL and LDL were normal. The nasopharyngeal swab for SARS-COV-2 was negative, while the serology test was positive for SARSCOV-2 (IgG>IgM). The lung ultrasound showed signs of interstitial disease in the parasternal site bilaterally, while the chest X-ray, the ECG and echocardiogram were normal. An antibiotic therapy with Ceftriaxone (100mg/kg/day iv) and a cortisone therapy with Methylprednisolone (1mg/kg/day iv) were performed for 5 days, with the progressive improvement of the general clinical conditions and blood tests, except for the increase of total cholesterol value and of IgG for SARS-COV-2 by more than 50% after 4-5 days upon entry.

Results

Table 1 shows the clinical signs at the onset for each case exposed. The common denominator is persistent fever associated, in case 1 with neurological impairment and in case 2 and in case 3, with Kawasaki syndrome-like symptoms; in no case there are gastrointestinal symptoms. As shown in Table 2, in all cases there is lymphocytopenia, an increase in phlogosis indices and ferritin levels and only in one case there is thrombocytopenia; the lipid profile shows a significant increase in triglyceride levels with normal total cholesterol values, as well as high density lipoprotein (HDL) and low-density lipoprotein (LDL). The nasopharyngeal swab for SARS-COV-2 was negative in all 3 cases, with positive serology to SARS-COV-2 both for IgM and IgG (IgG>IgM). In none of the three cases there were alterations in cardiac conduction, morphology and/or dynamics or any coronary lesions, nor there were lung lesions reported during the chest X-ray, while the lung ultrasound revealed signs of interstitial disease in the left parasternal site in case 1 and 2, and bilaterally in case 3. All 3 cases were treated with intravenous antibiotic and cortisone therapy; only in one case, such treatment was associated with intravenous immunoglobulins ev. In all cases, the course was benign with resolution of the symptoms detected upon admission within 4-5 days and normalization of both hemato chemical and instrumental parameters after about 1 month, associated to the increase by 50% of the IgG values revealed by the SARS-COV-2 serology test. Table 3 shows the lipid profile after 15 days from the onset, which highlights the reduction of triglyceride levels and increase of the total cholesterol value.

Table 1: Clinical signs at admission in the three cases

	Case 1	Case 2	Case 3
Fever	YES [maximum value: 39,5°C; range: every 4 hours; duration: 4 days]	YES [maximum value:38,5°C; range: every 7 hours; duration: 5 days]	YES [maximum value: 39°C;range: every 6 hours; duration: 5 days]
Lymphadenopathy	NO	YES	NO
Features KS like	NO	YES	YES
Aspecific rash	NO	YES	YES
Upper respiratory tract infection	NO	NO	YES
Cardiac symptoms	YES	YES	YES
Gastrointestinal symptoms	NO	NO	NO
Neurologic symptoms	YES	NO	NO
KS = Kawasaki syndrome			

Table 2: Lab tests upon admission in the three cases

	Values Case 1 (n.v.)	Values Case 2 (n.v.)	Values Case 3 (n.v.)
CRP mg/dl	**11,78** (0-0,5)	**6,75** (0-0,5)	**15,61** (0-0,5)
Procalcitonin (ng/ml)	**0,4** (0-0,5)	**0,8** (0-0,5)	**54** (0-0,5)
BNP (pg/ml)	**18416** (0-125)	**6236** (0-125)	**5286** (0-125)
Troponine (ng/L)	**0,8** (0-17,5)	**40,9** (0-17,5)	**6,4** (0-17,5)
D-Dimer (mg/L)	**1,55** (0-0,5)	**1.69** (0-0,5)	**7,88** (0-0,5)
IL-6 (ng/ml)	**17,1** (<0,04)	**21,8** (<0,04)	**18,6** (<0,04)
Ferritin (ng/ml)	**143** (20-200)	**701** (20-200)	**509** (20-200)
R.B.C. x 10^6/uL	**4.830** (4.200-5.500)	**4.200** (4.200-5.500)	**4.590** (4.200-5.500)
W.B.C. x 10^3/uL	**13.530** (4.000-11.000)	**11.630** (4.000-11.000)	**15.690** (4.000-11.000)
Hgb (g/dl)	11,7 (12-14)	11 (12-14)	**11,7** (12-14)
Platelets x 10 ^3/uL	**162000** (150000450000)	**92000** (150000450000)	**211000** (150000450000)
Total Cholesterol (mg/dl)	**142** (120-200)	**109** (120-200)	**138** (120-200)
HDL Cholesterol (mg/dl)	**17** (30-65)	**18** (30-65)	**8** (30-65)
LDL Cholesterol (mg/dl)	**65** (60-150)	**68** (60-150)	**50** (60-150)
Triglycerides (mg/dl)	**299** (30-110)	**226** (30-110)	**400** (30-110)
Fibrinogen (mg/dl)	**465** (180-360)	**447** (180-360)	**723** (180-360)
Lymphocytes (%)	**12** (23-48)	**21** (23-48)	**20** (23-48)
n.v. = normal values; BNP = B-type natriuretic peptide; CRP = C-Reactive Protein; IL-6 = Interleukin-6; R.B.C = Red Blood Cells; W.B.C = White blood cell; Hgb = Hemoglobin			

Table 3: Lipids profile after 15 days from clinical recovery phase

	Values Case 1 (n.v.)	Values Case 2 (n.v.)	Values Case 3 (n.v.)
Total Cholesterol (mg/dl)	265 (120-200)	236 (120-200)	199 (120-200)
HDL Cholesterol (mg/dl)	48 (30-65)	103 (30-65)	143 (30-65)
LDL Cholesterol (mg/dl)	189 (60-150)	99 (60-150)	37 (60-150)
Triglycerides (mg/dl)	139 (30-110)	171 (30-110)	95 (30-110)
n.v. = normal values			

Discussion and Conclusions

The consensus conference about PIMS (Paediatric Inflammatory Multisystem Syndrome Temporally Associated with SARS- CoV-2) distinguished the clinical presentation in 2 phenotypes: one of them is similar to a Kawasaki syndrome (either complete or incomplete), while the other one is non-specific, concerning those children reporting shock and/or fever and gastrointestinal, respiratory or neurological symptoms which are not matching the KS criteria [10]. Several authors presented different aspect of post-infection SARS-COV-2 syndrome, showing the wide variability of the clinical and phenotypic spectrum of MIS-C. Whittaker et al. described three different clinical patterns in 58 patients with MIS-C: one group reported shock with fever, biochemical signs of myocardial dysfunction that required inotropic and intensive care support; the second group showed Kawasaki syndrome signs according to the criteria of the American Heart Association, while the third group had persistent fever and increase of inflammatory markers without mucocutaneous signs of KS or organ dysfunction [11, 12]. Taffarel et al. described two clinical cases with cardiovascular dysfunction treated with invasive ventilation and vasoactive support, inflammatory parameters resulting fn laboratory tests with good response to treatments with intravenous immunoglobulins and corticosteroids, and general favourable course. Moreover, Licciardi F. et al. described the cases of 2 children where the SARS-Cov-2 infection lead to a Kawasaki–like hyperinflammatory syndrome with severe diarrhea [13].

Furthermore, in the research made by Leet PY et al. the clinical and laboratory characteristics of post-Sars-Cov-2 inflammatory syndrome in children and the response to treatment are retrospectively described, highlighting – besides the complete and/or incomplete clinical manifestations of the Kawasaki syndrome – the presence of cytokine production patterns and simultaneous detection of cytopenia, therefore concluding that MIS-C includes a wide range of phenotypic spectrum with clinical and laboratory characteristics which are different from the KS and the Macrophage Activation Syndrome (MAS) [14]. Covid-19 infection induces an acute phase response that also leads to lipid metabolism modification [15]. The increase in triglycerides is caused by an increase of VLDL secretion as a result of lipolysis, by an increase of free fatty acids hepatic synthesis and by the suppression of fatty acids oxidation, while blood cholesterol levels in adults tend to reduced and continue to decrease during hospitalization [16,17]. In this study, we analysed three clinical cases of MIS-C involving children under five years of age. In two of these, the symptoms at the onset were similar to KS, while in the third one the neurological involvement was prevalent. No association with gastrointestinal symptoms was found, while lymphocytopenia was constantly present and it was associated with a short-term thrombocytopenia only in one case. Cardiac involvement, despite the positivity of myocardial distress markers, was never documented, while lung ultrasound showed signs of mild interstitial disease, despite the scarcity of respiratory clinical signs. The course was favorable in all cases, with improvement in clinical conditions after about 5 days and normalization of phlogosis markers and lung involvement after about 30 days from the onset of symptoms. The lipid profile at the onset was characterised by an increase in triglyceride levels, suggesting a relation with the inflammatory indices, followed by an increase in the total cholesterol - probably connected to the immune response - after the healing phase, contrary to what has been stated by the current literature [18]. A longer follow-up is required to clarify the relationship between the changes in the lipid profile, the inflammatory state and the immune response.

List of Abbreviations

MIS-C: multisystem inflammatory syndrome in children;
KS: Kawasaki syndrome;
HDL: high density lipoprotein;
LDL: low density lipoprotein;
ECG: electrocardiogram;
IGG: Immunoglobulin G;
IGM: immunoglobulin M;
CRP: C-reactive protein;
NT-proBNP: n-terminal pro-B-type natriuretic peptide;
CRP: C reactive protein
IL-6: interleukin 6;
R.B.C.: red blood cell;
W.B.C.: white blood cell;
Hb: haemoglobin;
T cholesterol: Total cholesterol.
MAS: Macrophage Activation Syndrome

Declarations

Ethical approval and consent to participate
Not applicable

Consent for publication

The patients' parents provided their consent to submission

Availability of data and material

Not applicable

Competing interests

The authors declare that they have no competing interests

Funding

None of the authors participating in the drafting of this case report has been sponsored

Authors' contributions

All authors participated in drafting the manuscript and managed the patients' follow-up.
All authors read and approved the final manuscript.

Acknowledgements

Not applicable

References

1. Consiglio, C. R., Cotugno, N., Sardh, F., Pou, C., Amodio, D., Rodriguez, L., ... & CACTUS Study Team. (2020). The immunology of multisystem inflammatory syndrome in children with COVID-19. Cell, 183(4), 968-981.

2. Rajapakse, N., & Dixit, D. (2021). Human and novel coronavirus infections in children: a review. Paediatrics and international child health, 41(1), 36-55.
3. Radia, T., Williams, N., Agrawal, P., Harman, K., Weale, J., Cook, J., & Gupta, A. (2021). Multi-system inflammatory syndrome in children & adolescents (MIS-C): A systematic review of clinical features and presentation. Paediatric respiratory reviews, 38, 51-57.
4. Esposito, S., & Principi, N. (2021). Multisystem inflammatory syndrome in children related to SARS-CoV-2. Pediatric Drugs, 23(2), 119-129.
5. Riollano-Cruz, M., Akkoyun, E., Briceno-Brito, E., Kowalsky, S., Reed, J., Posada, R., ... & Paniz-Mondolfi, A. (2021). Multisystem inflammatory syndrome in children related to COVID-19: A New York City experience. Journal of Medical Virology, 93(1), 424-433.
6. Nogueira-de-Almeida, C. A., Ciampo, L. A. D., Ferraz, I. S., Ciampo, I. R. L. D., Contini, A. A., & Ued, F. D. V. (2021). Pediatric multisystem inflammatory syndrome associated with COVID-19: urgent attention required. Revista da Associação Médica Brasileira, 67, 115-120.
7. Feldstein, L. R., Rose, E. B., Horwitz, S. M., Collins, J. P., Newhams, M. M., Son, M. B. F., ... & Randolph, A. G. (2020). Multisystem inflammatory syndrome in US children and adolescents. New England Journal of Medicine, 383(4), 334-346.
8. Abdel-Haq, N., Asmar, B. I., Deza Leon, M. P., McGrath, E. J., Arora, H. S., Cashen, K., ... & Ang, J. Y. (2021). SARS-CoV-2-associated multisystem inflammatory syndrome in children: clinical manifestations and the role of infliximab treatment. European journal of pediatrics, 180(5), 1581-1591.
9. Lami, F., Scalabrini, I., Lucaccioni, L., & Iughetti, L. (2020). The "perfect" storm: Current evidence on pediatric inflammatory multisystem disease during SARS-CoV-2 pandemic. Acta Bio Medica: Atenei Parmensis, 91(3), e2020034.
10. Harwood, R., Allin, B., Jones, C. E., Whittaker, E., Ramnarayan, P., Ramanan, A. V., ... & Yardley, I. (2021). A national consensus management pathway for paediatric inflammatory multisystem syndrome temporally associated with COVID-19 (PIMS-TS): results of a national Delphi process. The Lancet Child & Adolescent Health, 5(2), 133-141.
11. Safadi, M. A. P., & Silva, C. A. A. D. (2020). The challenging and unpredictable spectrum of COVID-19 in children and adolescents. Revista Paulista de Pediatria, 39.
12. Newburger, J. W., Takahashi, M., Gerber, M. A., Gewitz, M. H., Tani, L. Y., Burns, J. C., ... & Taubert, K. A. (2004). Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. Circulation, 110(17), 2747-2771.
13. Lee, P. Y., Day-Lewis, M., Henderson, L. A., Friedman, K. G., Lo, J., Roberts, J. E., ... & Son, M. B. F. (2020). Distinct clinical and immunological features of SARS–CoV-2–induced multisystem inflammatory syndrome in children. The Journal of clinical investigation, 130(11), 5942-5950.
14. Khovidhunkit, W., Kim, M. S., Memon, R. A., Shigenaga, J. K., Moser, A. H., Feingold, K. R., & Grunfeld, C. (2004). Effects of infection and inflammation on lipid and lipoprotein metabolism: mechanisms and consequences to the host. The Journal of Lipid Research, 45(7), 1169-1196.
15. Kočar, E., Režen, T., & Rozman, D. (2021). Cholesterol, lipoproteins, and COVID-19: Basic concepts and clinical applications. Biochimica et Biophysica Acta (BBA)-Molecular and Cell Biology of Lipids, 1866(2), 158849.
16. Feingold K R, Anawalt B, Boyce A et al. Lipid and lipotrotein levels in patients with COVID19 infections. In: endotext (internet), South Dartmounth (MA), MD Ttextcom, inc: 2000-2020 Nov 15.
17. Bermudes A C G, deCarvlho W B, Zamberlan P, Muramoto G, Maranhao R C, Delgado A F. Changes in lipoid metabolism in pediatric patients with severe sepsis and septic shock. Nutrition 2018 Mar; 47: 104-109.